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EXAMINER	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 010104

Application Number: 09/626,616
Filing Date: July 27, 2000
Appellant(s): YU, LEI

Mark Wilson
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 11/7/03.*(1)* ***Real Party in Interest***

A statement identifying the real party in interest is contained in the brief.

(2) ***Related Appeals and Interferences***

The brief does not contain a statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief. Therefore, it is presumed that there are none. The Board, however, may exercise its discretion to require an explicit statement as to the existence of any related appeals and interferences.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is substantially correct. The changes are as follows: the rejection of claims 86-90, 92-99 and 101 under 35 USC 112, second paragraph, regarding the term "including the guanine at position 389" has been withdrawn in view of Appellants' arguments.

(7) Grouping of Claims

Appellant's brief includes a statement that claims 83-101 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

No prior art is relied upon by the examiner in the rejection of the claims under appeal.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112, first paragraph – written description

Claims 86-90, 92-99 and 101 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. Claims 86-90 recite a process for screening a candidate substance for its ability to bind to a mu opioid receptor wherein the receptor is encoded for by a nucleic acid molecule comprising at least 35, 45, 50, 75, or 100 contiguous nucleotides of SEQ ID NO:7, including the guanine at position 389, by detecting the ability of the candidate substance to bind the opioid receptor polypeptide. Claim 93 recites the process of claim 86 wherein the opioid receptor is chimeric. Claims 94-99 recite a process for screening a candidate substance for its ability to bind to *any* opioid receptor wherein the receptor is encoded for by a nucleic acid molecule comprising at least 35, 45, 50, 75, or 100 contiguous nucleotides of SEQ ID NO:7, including the guanine at position 389, by detecting the ability of the candidate substance to bind the opioid receptor polypeptide. Claim 101 recites the process of claim 94 wherein the opioid receptor is chimeric.

However, the nucleic acid molecules encoding at least 35, 40, 45, 50, 75, or 100 contiguous nucleotides of SEQ ID NO:7, which are used in these screening methods, would have one or more nucleic acid substitutions, deletions, insertions and/or additions to the nucleic acid molecule of SEQ ID NO:7, and would encode for proteins with one or more amino acid substitutions, deletions, insertions and/or additions to the protein encoded for by SEQ ID NO:7.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Structural features that could distinguish compounds in the genus from others in the nucleic acid or protein class are missing from the disclosure. Appellant is claiming a process for screening a compound its ability to bind opioid receptors. However, Appellant has provided no written description as to what amino acid residues of these receptors are necessary in order to retain the ligand-binding characteristics of these opioid receptors (i.e. recitation of a binding domain), or as to what other residues are necessary to produce a functional opioid receptor. The protein encoded for by SEQ ID NO:7 (SEQ ID NO:8) is the only protein which has been described in the present specification which meets the limitations of claims 86-90, 92-99 and 101. Furthermore, the protein of SEQ ID NO:8 is 400 amino acid residues in length. However, the claims recite using polypeptides which encode as few as 12 amino acids

of the protein of SEQ ID NO:8. Again, the Appellant has provided no written description as to what amino acid residues are necessary for ligands to bind to these opioid receptors, or as to what other residues are necessary to produce functional opioid receptors. These claims are reciting a process for screening opioid receptors (i.e. full-length receptors), and not for screening *fragments* of opioid receptors, which are encompassed by proteins encoded for by at least 35, 45, 50, 75, or 100 contiguous bases of SEQ ID NO:7. Apart from the length of the claimed polypeptides (35, 45, 50, 75, 100 bases), the only common structural attribute which identifies the members of the claimed genus of nucleic acid molecules and proteins is that they must comprise the guanine at position 389 of SEQ ID NO:7. Example VI, on page 121 of the specification discloses that the this guanine residue produces a 10-fold increase in affinity in dynorphin A (1-17) binding compared to the protein of Wang et al., which is encoded for by a nucleic acid molecule which does not comprise a guanine at position 389 of SEQ ID NO:7. However, the general knowledge and level of skill in the art do not supplement the omitted description of what amino acid residues are necessary to produce a functional opioid receptor because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, "35, 45, 50, 75, or 100 contiguous bases of SEQ ID NO:7 including guanine 389" alone is insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Appellant was not in possession of the claimed genus at the time the invention was made. Claim 92 is rejected since it depends from rejected claim 86.

Claim Rejections - 35 USC § 112, first paragraph – enablement

Claims 86-90, 92-99 and 101 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for screening a candidate substance for its ability to bind to an opioid receptor encoded for by a nucleic acid molecule comprising SEQ ID NO:7 in its entirety, as well as screening a candidate substance for its ability to bind to chimeric opioid receptors comprising SEQ ID NO:7 in its entirety, does not reasonably provide enablement for a process for screening a candidate substance for its ability to bind to an opioid receptor encoded for by a nucleic acid molecule comprising at least 35, 45, 50, 75, or 100 contiguous nucleotides of SEQ ID NO:7, including the guanine at position 389, nor does the specification provide enablement for screening a candidate substance for its ability to bind to chimeric opioid receptors comprising said contiguous nucleotides. The specification

does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive with regard to screening a candidate substance for its ability to bind to an opioid receptor encoded for by a nucleic acid molecule comprising at least 35, 45, 50, 75, or 100 contiguous nucleotides of SEQ ID NO:7, including the guanine at position 389 as well as to screening a candidate substance for its ability to bind to chimeric opioid receptors comprising said contiguous nucleotides. Nucleic acid molecules comprising as few as 35 contiguous bases of SEQ ID NO:7 would have one or more nucleic acid substitutions, deletions, insertions and/or additions to said polynucleotides. Similarly, the proteins encoded for by these nucleic acid molecules would encode for proteins with one or more amino acid substitutions, deletions, insertions and/or additions to the protein encoded for by SEQ ID NO:7.

Other than that encoded for by SEQ ID NO:7, Appellants provide no guidance or working examples of opioid receptor which are encoded for by as few as 35 contiguous bases of SEQ ID NO:7, nor is it predictable to one of ordinary skill in the art how to make a functional opioid receptor given that the receptor only needs to comprise anywhere from 11-33 contiguous amino acids of SEQ ID NO:8 (i.e. 35-100 contiguous bases of SEQ ID NO:7). Furthermore, claim 86 recites a process for screening a candidate compound for its ability to bind a mu opioid receptor, whereas claim 94 recites a process for screening a candidate compound for its ability to bind *any* opioid receptor. Again, the only guidance that the Appellant has provided in making an opioid receptor for use in the claimed screening process is that it must be encoded for by at least 35 contiguous bases of SEQ ID NO:7. Not only has the Appellant not taught the artisan how to make a functional *mu* opioid receptor encoded for by less than the full-length of SEQ ID NO:7 (claim 86), but the Appellant has not taught the artisan how to produce *any* opioid receptor encoded for by less than the full-length of SEQ ID NO:7 (claim 94). Claim 94 encompasses a process of screening a compound for its ability to bind to any opioid receptor, not just the mu opioid receptor. However, the only limitation in both independent claims 86 and 94 is that the opioid receptor must be encoded for by at least 35 contiguous bases of SEQ ID NO:7 and include the guanine at position 389 of SEQ ID NO:7. Based on this information, the requirements to produce a mu opioid receptor are exactly

the same as to produce a non-mu opioid receptor. Therefore, given that the opioid receptor must comprise only as few as 11-33 amino acid resides of SEQ ID NO:8, the artisan is not able to distinguish between making a mu opioid receptor and making any other opioid receptor.

In summary, the breadth of the claims is excessive with regard to Appellants claiming a process for screening a candidate substance for its ability to bind to an opioid receptor encoded for by a nucleic acid molecule comprising only at least 35, 45, 50, 75, or 100 contiguous nucleotides of SEQ ID NO:7, including the guanine at position 389, as well as screening a candidate substance for its ability to bind to chimeric opioid receptors comprising said contiguous nucleotides. There is a lack of guidance and working examples of these nucleic acid molecules and proteins, as well as how to differentiate making mu opioid receptors from making non-mu opioid receptors. Appellants do not provide any language in the claims, or specification, which would allow the artisan to make a functional opioid receptor, either mu or non-mu opioid receptors by using as few as 35 contiguous bases of SEQ ID NO:7. The fact that the nucleic acid molecules encoding these receptors must comprise the guanine at position 389 of SEQ ID NO:7 is, itself, insufficient. These factors, along with the lack of predictability to one of ordinary skill in the art as to how to differentially make a functional opioid receptor, as well as how to make both mu and non-mu opioid receptors, leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed. Claim 92 is rejected since it depends from rejected claim 86.

(11) Response to Argument

Claim Rejections - 35 USC § 112, first paragraph – written description

Appellants argue that one skilled in the art would reasonably conclude that the inventor had possession of a recombinant opioid receptor polypeptide encoded for by a nucleic acid sequence comprising at least 35 contiguous nucleotides of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7 based on the description provided for in the specification at least on pages 36 to 44; pages 150-153, and by SEQ ID NO:7 and SEQ ID NO:8. They further argue that the Examiner, "in requiring that the recombinant opioid receptor polypeptide recited in the claims be a full-length opioid receptor, has not only failed to broadly interpret Appellant's claims, but has improperly interpreted the claims in an unreasonably narrow manner and that none of the claims require that the process for screening a candidate substance utilize a full-length, functional mu opioid receptor." Appellant asserts that the claims are not for opioid receptors, but rather are for processes of screening substances for the ability to bind to an opioid receptor and that there is nothing in the claims to limit the candidate substance to a ligand.

These arguments have been considered, but are not deemed persuasive. First, one skilled in the art would reasonably conclude that the inventor had possession of a recombinant opioid receptor polypeptide encoded for by a nucleic acid sequence comprising SEQ ID NO:7, but not for any and all polypeptides encoded by at least 35 contiguous nucleotides of SEQ ID NO:7. The specification provides a written description of only SEQ ID NO:7. No other species are described, or structurally contemplated, within the instant specification. Therefore, one skilled in the art cannot reasonably visualize or predict critical nucleic acid residues which would structurally characterize the genus of nucleic acids encoding the genus of mu opioid receptors claimed, because it is unknown and not described what structurally constitutes any different nucleic acids encoding these receptors, or nucleic acids encoding mu opioid receptors from any different species, which are further not described; thereby not meeting the written description requirement under 35 USC 112, first paragraph. Though the claims are drawn to methods of screening candidate substances and none of the claims require the use of a full-length receptor, the claims still read on the full-length receptor. The claims lack adequate written description of these other receptors. As argued on pages 2-3 of the Office Action dated 12/31/02, though Applicant is claiming a method of using opioid receptors and not the receptors themselves, the claims recite a process for screening a substance's ability to bind to a mu opioid receptor. Therefore, in order to practice the claimed invention, one of ordinary skill in the art would need to be able to first identify a full-length mu opioid receptor which comprises at least 35 contiguous bases of SEQ ID NO:7. Given the only limitation that the receptor has to be encoded for by a nucleic acid molecule comprising these bases and include guanine 389, the artisan is not provided enough description as to what constitutes a mu opioid receptor. Polynucleotides encoding opioid receptors, including SEQ ID NO:7, are approximately 1600 bases in length. Therefore, to claim a method of using an opioid receptor by providing the limitation that it must comprise 35 of these 1600 bases is insufficient to demonstrate that Applicant was in possession of any of these receptors other than that encoded for by SEQ ID NO:7. Furthermore, the argument that the binding characteristics are not relevant since this receptor can bind antibody is also not persuasive for these reasons. If Applicant's intentions were to screen for antibodies, then the claim should be drawn to screening for the ability of an antibody to bind a *fragment* of a mu opioid receptor encoded for by 35 contiguous bases of SEQ ID NO:7. **However, without proper support, this would be considered new matter**. It is believed that all pertinent arguments have been addressed.

Claim Rejections - 35 USC § 112, first paragraph - enablement

A. Appellant submits that the application contains sufficient description to enable one skilled in the art to make and use the claimed invention without unduly extensive experimentation and that the claimed processes do not require that the recombinant opioid receptor polypeptide be a full-length opioid receptor. Rather, the claims provide a recombinant opioid receptor polypeptide encoded by a nucleic acid sequence comprising at least 35 contiguous nucleotides of SEQ ID NO:7, including the guanine at nucleotide 389 of SEQ ID NO:7. Furthermore, Appellants argue that the specification teaches the making and using of recombinant opioid receptor polypeptides, particularly chimeras, at least on pages 36-44. Also, numerous references cited within the specification describe methods of manipulating G-protein receptors known to those of skill in the art, such as adrenergic receptors. Thus, the preparation and use of a wide variety of recombinant opioid receptor polypeptides encoded by a nucleic acid sequence comprising at least 35 contiguous nucleotides of SEQ ID NO:7, including the guanine at nucleotide 389 of SEQ ID NO:7, was taught or known to one of skill in the art.

These arguments have been considered, but are not deemed persuasive. As stated on pages 3-4 of the Office Action dated 12/31/02, the claims recite a process for screening a candidate opioid receptor for its ability to bind an opioid receptor, including a mu opioid receptor. The claims read on any full-length opioid receptor comprising at least 35 contiguous bases of SEQ ID NO:7. Regardless of whether or not the present invention is simply being used to identify antibodies which bind the receptor, or even if the claims are drawn to methods of screening compounds, and not to the receptors themselves, the claims still recite "mu opioid receptor" implying that the artisan would know how to make a full-length, functional mu opioid receptor given the guidance in the specification and claims that the receptor must only comprise as few as 35 contiguous bases of SEQ ID NO:7. Polynucleotides encoding opioid receptors, including SEQ ID NO:7, are approximately 1600 bases in length and Appellant has provided no guidance and working examples of any opioid receptor which is only as small as 35 contiguous bases of SEQ ID NO:7 other than SEQ ID NO:7 itself, nor is it predictable to one of ordinary skill in the art how to make a functional opioid receptor given that the receptor only needs to comprise anywhere from 11-33 contiguous amino acids of SEQ ID NO:8 (i.e. 35-100 contiguous bases of SEQ ID NO:7). The fact that numerous references cited within the specification describe methods of manipulating G-protein receptors known to those of skill in the art, such as adrenergic receptors is also not persuasive since the claims and specification of the present invention are not manipulating G protein-coupled receptors, since Appellants have not taught the artisan how to make a G protein-coupled receptor having as few as 35 contiguous bases. Furthermore, the structural elements (e.g. critical amino acid residues) of adrenergic receptors, as

argued by Appellants, would be expected to be different than for those to make functional opioid receptors. In order to manipulate the receptors of the art as well as of the present invention, the artisan would first need to know how to make these receptors, which is not taught in the specification. It is believed that all pertinent arguments have been addressed.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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January 7, 2004

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